

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1, 6-11 and 18-27 are pending in the application, with 1 and 23 being the independent claims. The Examiner has indicated that claims 23-27 are allowed. Claims 2-5 and 12-17 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claim 1 has been amended. Support for the amendment to claim 1 may be found, *inter alia*, in the specification at paragraphs [0006], [0059], and [0061].

Applicants submit that this amendment places the application in a condition for allowance and does not raise any new issue requiring further search or consideration. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 112 (1st Paragraph)

The Examiner has rejected claims 1-22 under 35 USC § 112, 1st paragraph for allegedly failing to comply with the written description requirement. The Examiner alleges that Applicants have not pointed to any passage of the specification to support the limitation "does not require vortexing." Paper No. 20060821, page 2. Applicants respectfully disagree.

In the reply filed June 29, 2006, Applicants pointed to the Examples as support for the limitation that the claimed method "does not require vortexing." Reply filed June 29, 2006, page 8. Vortexing is not required in any of the methods exemplified in the Examples. Additionally, Applicants cited *In re Wertheim*, 541 F.2d 257, 263 (C.C.P.A. 1976) and *In re Johnson*, 588 F.2d 1008, 1017 (C.C.P.A. 1977) in support of the notion that negative limitations need not be present *in haec verba* in the specification to be fully supported. Reply filed June 29, 2006, page 8, fn 1.

However, solely in an effort to advance prosecution, and not acquiescing in the propriety of the rejection, Applicants have amended claim 1, from which claims 6-11 and 18-22 depend, to remove the phrase "does not require vortexing." Additionally, claims 2-5 and 12-17 have been canceled. As such Applicants believe that the Examiner's rejection is now moot and request that the Examiner withdraw the rejection.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 1-22 under 35 USC § 103(a) for allegedly being unpatentable over International Published Application No. WO 02/00844 ("Evans") in view of U.S. Patent No. 5,811,088 ("Hunter"). Paper No. 20060821, page 3. Applicants respectfully traverse this rejection as it may apply to the currently pending claims.

The Examiner alleges that there is no requirement for vortexing in the disclosure of Evans, and one of ordinary skill in the art could substitute vortexing for any mixing technique as a design choice. Paper No. 20060821, page 6. Applicants respectfully disagree. Evans clearly teaches that the preparation of the CRL-1005 formulations

containing DNA and BAK, as used in the Examples of the application, teach vortexing the solution to obtain a formulation with a particle size in the range of 200-500 nm. *See* WO 02/00844, page 32, line 23 - page 33, line 9. Indeed the BAK, CRL 1005 and DNA solution, as described in Evans, is vortexed "to solublize the polymer" and then after addition of BAK "vortexed extensively" and then vortexed every time the temperature of the solution was allowed to increase from ~2°C to above the cloud point until the particles were in the range of 200-500nm. *See Id.* As such, one of ordinary skill in the art would have thought that vortexing was required to achieve the desired particles in the formulations disclosed in WO 02/00844.

However, solely in an effort to advance prosecution, and not acquiescing in the propriety of the rejection, Applicants have amended claim 1, from which claims 6-11 and 18-22 depend, to recite "wherein said method does not include thermal cycling of the mixture above and below the cloud point of said block copolymer." Claims 2-5 and 12-17 have been canceled.

As amended, the presently claimed methods are directed to mixing a cationic surfactant, a polyoxyethylene (POE) and polyoxypropylene (POP) block copolymer, and a polynucleotide at a temperature below the cloud point of said block copolymer to form a mixture, without thermal cycling the mixture above and below the cloud point of said block copolymer, and cold filtering the mixture to produce a sterile formulation. Examples 2 and 8 of the present application describe the production of sterile formulations using the method of claim 1.

Evans does not teach a method of producing a cationic surfactant, block copolymer and polynucleotide formulation without thermal cycling. Indeed, the Examiner has stated that Evans

taught methods of formulating DNA vaccines by mixing a cationic surfactant such as benzalkonium chloride (BAK), a polyoxypropylene (POP)-polyoxyethylene (POE) copolymer such as CRL 1005, and a polynucleotide at a temperature below the cloud point of the copolymer (about 2-7°C), repeatedly cycling the temperature of the mixture above and below the cloud point of the copolymer. See paragraph bridging pages 32 and 33.

Paper No. 20060821, p. 3. In addition, Evans does not teach cold filtering of the mixture to produce a sterile formulation. Therefore, Evans is deficient as a primary reference upon which to base a *prima facie* case of obviousness.

These deficiencies are not cured by the disclosure of Hunter. Hunter does not disclose, suggest or otherwise contemplate a method of producing a sterile cationic surfactant, block copolymer and polynucleotide formulation without the need for thermal cycling. As such, taken together Evans and Hunter do not teach all elements of the claimed invention as amended. Thus, this combination of references is clearly insufficient to establish a *prima facie* case of obviousness. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has also rejected claim 9 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Evans and Hunter as applied to claims 1-8 and 11-22 above, and further in view of U.S. Patent 6,933,286 ("Emanuele"). Applicants respectfully traverse this rejection.

As stated *supra*, Evans and Hunter do not teach all elements of the currently pending claims. Emanuele does not cure the deficiencies of Evans and Hunter because the combined cited references still do not teach or suggest the production of cationic, block copolymers and polynucleotide compositions without the need for thermal cycling. Indeed, Emanuele teaches POP-POE-POP block copolymers and polynucleotide formulations however there is no teaching with regard to the addition of cationic surfactants. As such, Applicants respectfully assert that a *prima facie* case of obviousness has not been established and respectfully request that the Examiner reconsider and withdraw the rejection.


Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: December 4, 2006

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